

**IN THE CLAIMS**

This listing of claims will replace all prior versions and listings of the claims in the present application.

1-12. **(Cancelled)**

13. **(Currently Amended)** A method for inducing or enhancing the glucose-responsiveness of a ~~pancreatic islet or~~ pancreatic cell, which ~~pancreatic islet or~~ cell has impaired ~~islet~~ cell function and which ~~islet~~ cell function is glucose-responsiveness, comprising administering to the ~~pancreatic islet or~~ pancreatic cell a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a ~~corresponding sequence~~ identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to induce or enhance the glucose-responsiveness of the pancreatic ~~islet or~~ cell, and wherein said PYY agonist or biologically active fragment ~~has one or more of the following functions of PYY:~~

- ~~(a) — binds a PYY receptor;~~
- ~~(b) — promotes glucose-responsiveness of ~~pancreatic islets or~~ the pancreatic ~~cells;~~ cell.~~
- ~~(c) — inhibits intestinal motility;~~
- ~~—— (d) — inhibits mesenteric blood flow;~~
- ~~—— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) — stimulates net absorption of nutrients.~~

14. **(Cancelled)**

15. **(Currently Amended)** The method of claim 13, whereby administration of the PYY agonist causes the ~~islet or~~ cell to produce insulin when treated with glucose.
16. **(Currently Amended)** The method of claim 13, wherein the ~~islet~~ cell is a fetal islet cell.
17. **(Original)** The method of claim 13, wherein the cell is a fetal pancreatic cell.
18. **(Currently Amended)** The method of claim 13, wherein the ~~islet~~ cell is a ~~postpartum~~ postpartum islet cell.
19. **(Currently amended)** The method of claim 13, wherein the cell is a ~~postpartum~~ postpartum cell.
20. **(Previously presented)** The method of claim 13, wherein the cell is a pancreatic  $\beta$  cell.
21. **(Currently Amended)** A method for inducing or enhancing glucose metabolism in an animal having a disease associated with abnormal glucose metabolism, comprising administering to the animal an amount of a composition including a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a ~~corresponding sequence identical to a peptide encoded by a nucleic acid sequence~~ wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, and wherein the amount of said PYY agonist or biologically active fragment thereof is therapeutically effective to induce or enhance glucose metabolism in the animal, and wherein said PYY agonist or biologically active fragment thereof ~~has one or more of the following functions of PYY:~~
- (a)—— binds a PYY receptor;

- ~~—— (b) — promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (e) — inhibits intestinal motility;~~
- ~~—— (d) — inhibits mesenteric blood flow;~~
- ~~—— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) — stimulates net absorption of nutrients.~~

22. (Cancelled)

23. (Currently Amended) A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism an amount of a composition comprising a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a corresponding sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, and wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to treat the disease, and wherein said PYY agonist or biologically active fragment ~~has one or more of the following functions of PYY:~~

- ~~—— (a) — binds a PYY receptor;~~
- ~~—— (b) — promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (e) — inhibits intestinal motility;~~
- ~~—— (d) — inhibits mesenteric blood flow;~~
- ~~—— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) — stimulates net absorption of nutrients.~~

24-27. (Cancelled)

28. **(Previously presented)** The method of claim 23, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.
29. **(Previously presented)** The method of claim 23, wherein said disease is Type II diabetes mellitus (NIDD).
30. **(Previously presented)** The method of any one of claims 13 and 15-20, wherein said PYY agonist is administered together with a dipeptidylpeptidase inhibitor, insulin, or GLP-1.
31. **(Previously presented)** The method of any one of claims 13 and 15-20, wherein said PYY agonist is conjointly administered either simultaneously, sequentially, or separately with a dipeptidylpeptidase inhibitor, insulin, or GLP-1.
32. **(Previously presented)** The method of claim 30, wherein said dipeptidylpeptidase inhibitor is DPIV.
33. **(Currently Amended)** A method for maintaining or restoring a function of a pancreatic  $\beta$  cell cells, wherein the function is glucose responsivity or glucose sensing, comprising administering to a ~~pancreatic islet or~~ pancreatic cell, which ~~pancreatic islet or~~ pancreatic cell has impaired glucose responsivity or glucose sensing, a composition comprising a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a ~~corresponding~~ sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore the function of said

pancreatic  $\beta$  cell cells, and wherein said PYY agonist or biologically active fragment ~~has one or more of the following functions of PYY:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

34-38. (Cancelled)

39. (Previously presented) The method of any of claims 13 and 15-20, wherein said PYY agonist enhances or recovers glucose responsiveness.

40-44. (Cancelled)

45. (Currently Amended) A method for maintaining or restoring normal pancreatic islet function to a pancreatic islet or cell having impaired pancreatic islet cell function, wherein the function is glucose responsivity or glucose sensing, comprising administering to a cultured pancreatic islet or cell having altered pancreatic islet cell function a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a ~~corresponding sequence identical to a peptide encoded by a~~ nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore normal pancreatic islet

cell function to a pancreatic ~~islet or cell~~ having altered pancreatic ~~islet~~ cell function, and wherein said PYY agonist or biologically active fragment ~~has one or more of the following functions of PYY:~~

- ~~— (a) — binds a PYY receptor;~~
- ~~— (b) — promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~— (c) — inhibits intestinal motility;~~
- ~~— (d) — inhibits mesenteric blood flow;~~
- ~~— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~— (f) — stimulates net absorption of nutrients.~~

46. **(Currently Amended)** The method of claim 45, ~~where in said~~ wherein the pancreatic ~~islet~~ cell is a failing  $\beta$  cell.

47-49. **(Cancelled)**

50. **(Currently Amended)** The method of claim 21, wherein said animal is selected from the group consisting of a human and a rat.

51-52. **(Cancelled)**

53. **(Previously presented)** The method of claim 17, wherein the cell is a pancreatic  $\beta$  cell.

54. **(Previously presented)** The method of claim 19, wherein the cell is a pancreatic  $\beta$  cell.

55-56. **(Cancelled)**

57. **(Previously presented)** The method of claim 21, wherein said composition further comprises a dipeptidylpeptidase inhibitor, insulin or GLP-1.

58. **(Previously presented)** The method of claim 21, wherein said composition is conjointly administered either simultaneously, sequentially or separately with a dipeptidylpeptidase inhibitor, insulin or GLP-1.

59. **(Previously presented)** The method of claim 23, wherein said composition further comprises a dipeptidylpeptidase inhibitor, insulin or GLP-1.

60. **(Previously presented)** The method of claim 23, wherein said composition is conjointly administered either simultaneously, sequentially or separately with a dipeptidylpeptidase inhibitor, insulin or GLP-1.

61-75. **(Cancelled)**

76. **(Previously presented)** The method of claim 23, wherein said PYY agonist enhances or recovers glucose responsiveness.

77. **(Previously presented)** The method of claim 21, wherein said PYY agonist enhances or recovers glucose responsiveness.

78. **(Previously presented)** The method of claim 33, wherein said PYY agonist enhances or recovers glucose responsiveness.

79-84. **(Cancelled)**

85. **(Currently Amended)** The method of claim 23, wherein said animal is selected from the group consisting of a human and a rat.

86. **(Cancelled)**

87. **(Currently Amended)** A method for inducing or enhancing the glucose-responsiveness of a pancreatic ~~islet or cell~~, which pancreatic ~~islet or cell~~ has impaired glucose-responsiveness, comprising administering to the pancreatic ~~islet or cell~~ a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to induce or enhance the glucose-responsiveness of the pancreatic ~~islet or cell~~, wherein the PYY or biologically active fragment thereof ~~has one or more of the following functions:~~

- ~~——(a)——~~ binds a PYY receptor;
- ~~——(b)——~~ ~~promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~——(c)——~~ ~~inhibits intestinal motility;~~
- ~~——(d)——~~ ~~inhibits mesenteric blood flow;~~
- ~~——(e)——~~ ~~mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~——(f)——~~ ~~stimulates net absorption of nutrients.~~

88. **(Currently Amended)** A method for inducing or enhancing glucose metabolism in an animal having a disease associated with abnormal glucose metabolism, comprising administering to the animal an effective amount of a composition including a PYY or a biologically active fragment thereof, wherein the amount of PYY or a biologically active fragment thereof is effective to induce or enhance glucose responsiveness in the animal, thereby inducing or enhancing glucose metabolism in the animal, and wherein the PYY or biologically active fragment thereof ~~has one or more of the following functions:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

89. **(Currently Amended)** A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism an amount of a composition comprising a PYY or a biologically active fragment thereof, wherein the amount of PYY or a biologically active fragment thereof is sufficient to treat the disease in the animal, and wherein the PYY or biologically active fragment thereof ~~has one or more of the following functions:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

90. **(Currently Amended)** A method for maintaining or restoring a function of a pancreatic  $\beta$  cell ~~cells~~, wherein the function is glucose responsivity or glucose sensing, comprising administering to a ~~pancreatic islet or pancreatic cell~~, which ~~pancreatic islet or pancreatic cell~~ has impaired glucose responsivity or glucose sensing, a composition comprising a PYY or a

biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain or restore the function of said pancreatic  $\beta$  cell-cells, wherein the PYY or biologically active fragment thereof ~~has one or more of the following functions:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

91. **(Currently Amended)** A method for maintaining or restoring normal pancreatic ~~islet~~ cell function, wherein the function is glucose responsivity or glucose sensing, comprising administering to a cultured ~~pancreatic islet or pancreatic cell~~, which ~~pancreatic islet or pancreatic cell~~ has impaired glucose responsivity or glucose sensing, a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain or restore normal pancreatic ~~islet~~ cell function, wherein the PYY or biologically active fragment thereof ~~has one or more of the following functions:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~

~~— (f) — stimulates net absorption of nutrients.~~

92. **(Currently Amended)** A method for maintaining glucose-responsiveness of a pancreatic islet or pancreatic cells cell, comprising contacting the pancreatic islet or cells cell, which pancreatic islet or pancreatic cell has impaired glucose responsivity or glucose sensing, with a composition comprising a PYY or a biologically active fragment thereof, wherein the amount of said PYY or biologically active fragment thereof is sufficient to maintain the glucose-responsiveness of the pancreatic islet or cells cell, wherein the PYY or biologically active fragment thereof, ~~has one or more of the following functions:~~

~~— (a) — binds a PYY receptor;~~

~~— (b) — promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~

~~— (c) — inhibits intestinal motility;~~

~~— (d) — inhibits mesenteric blood flow;~~

~~— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~

~~— (f) — stimulates net absorption of nutrients.~~

93. **(Currently Amended)** A method for maintaining glucose-responsiveness of a pancreatic islet or pancreatic cells cell, which pancreatic islet or pancreatic cells ~~have~~ cell has impaired glucose-responsiveness, comprising contacting the pancreatic islet or pancreatic cells cell with an effective amount of a composition comprising a PYY agonist or a biologically active fragment thereof, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain the glucose responsiveness of the pancreatic islet or cells cell, wherein said PYY agonist comprises an amino acid sequence having a ~~corresponding sequence identical to a~~ peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under

stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, and wherein said PYY agonist, or biologically active fragment, ~~has one or more of the following functions of PYY:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

94. **(Currently Amended)** A method for inducing, enhancing, or maintaining glucose-responsiveness of a pancreatic islet or pancreatic cells cell, which pancreatic islet or pancreatic cells ~~have~~ cell has impaired glucose-responsiveness, comprising contacting the pancreatic islet or pancreatic cells cell with an effective amount of a composition comprising a PYY agonist or a biologically active fragment thereof, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to induce, enhance, or maintain the glucose-responsiveness of the pancreatic islet or cells cell, wherein said PYY agonist comprises a polypeptide at least 70% identical with SEQ ID NO: 3, and wherein said PYY agonist, or biologically active fragment, ~~has one or more of the following functions of PYY:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~

~~— (e) — mediates gastric, pancreatic, or intestinal exocrine secretion; or~~

~~— (f) — stimulates net absorption of nutrients.~~

95. **(Cancelled)**

96. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 80% identical to SEQ ID NO: 3.

97. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 85% identical to SEQ ID NO: 3.

98. **(Previously presented)** The method of claim 94, wherein the PYY agonist comprises a polypeptide at least 90% identical to SEQ ID NO: 3.

99. **(Cancelled)**

100. **(Currently Amended)** The method of any of claims 92-94, wherein the pancreatic islet ~~or cells include~~ cell is a  $\alpha$ ,  $\beta$ ,  $\delta$ , or  $\phi$  cells  $\phi$ -cell.

101. **(Currently Amended)** The method of any of claims 92-94, wherein the pancreatic islet ~~or cells include~~ cell is an insulin-producing islet cells cell.

102. **(Currently Amended)** A method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism an amount of a composition comprising an effective amount of a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises a

polypeptide at least 70% identical to SEQ ID NO: 3, and wherein said PYY agonist, or biologically active fragment, ~~has one or more of the following functions of PYY:~~

- ~~—— (a) —— binds a PYY receptor;~~
- ~~—— (b) —— promotes glucose responsiveness of pancreatic islets or pancreatic cells;~~
- ~~—— (c) —— inhibits intestinal motility;~~
- ~~—— (d) —— inhibits mesenteric blood flow;~~
- ~~—— (e) —— mediates gastric, pancreatic, or intestinal exocrine secretion; or~~
- ~~—— (f) —— stimulates net absorption of nutrients.~~

103. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 80% identical to SEQ ID NO: 3.

104. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 85% identical to SEQ ID NO: 3.

105. **(Previously presented)** The method of claim 102, wherein the PYY agonist comprises a polypeptide at least 90% identical to SEQ ID NO: 3.

106. **(Previously presented)** The method of any of claims 102, 103 and 105, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.

107. **(Previously presented)** The method of any one of claims 102, 103 and 105, wherein said disease is hyperglycemia.

108. **(Previously presented)** The method of any one of claims 102 to 105, wherein said disease is obesity.
109. **(Previously presented)** The method of any one of claims 102, 103 and 105, wherein said disease is hyperlipidemia or hyperlipoproteinemia.
110. **(Previously presented)** The method of claim 23, wherein said disease is hyperglycemia.
111. **(Previously presented)** The method of claim 23, wherein said disease is obesity.
112. **(Previously presented)** The method of claim 23, wherein said disease is hyperlipidemia or hyperlipoproteinemia.
- 113-115. **(Cancelled)**
116. **(Previously presented)** The method of claim 89, wherein said disease is a condition selected from insulin resistance, glucose intolerance or glucose non-responsiveness.
117. **(Previously presented)** The method of claim 89, wherein said disease is hyperglycemia.
118. **(Previously presented)** The method of claim 89, wherein said disease is obesity.
119. **(Previously presented)** The method of claim 89, wherein said disease is hyperlipidemia or hyperlipoproteinemia.
120. **(Previously presented)** The method of any one of claims 89, 102, 103 and 105, wherein the composition further comprises GLP-1.

121. **(Previously presented)** The method of any one of claims 23, 89, 102, 103 and 105, wherein the treatment comprises nasal administration of the composition.

122. **(Currently Amended)** The method of any one of claims 23, 89, 102, 103 and 105, wherein the PYY agonist or fragment is PYY(3-36) of SEQ ID NO: 3.

123. **(Previously presented)** The method of claim 118, wherein the biologically active fragment is PYY(3-36), the composition comprises GLP-1, and the treatment comprises nasal administration of the composition.

124. **(New)** The method according to claim 13 wherein said PYY agonist or biologically active fragment also binds a PYY receptor.

125. **(New)** The method according to any one of claims 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also promotes glucose-responsiveness of pancreatic cells.

126. **(New)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also inhibits intestinal motility.

127. **(New)** The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also inhibits mesenteric blood flow.

128. (New) The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also mediates gastric, pancreatic, or intestinal exocrine secretion.

129. (New) The method according to any one of claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94, or 102 wherein said PYY agonist or biologically active fragment also stimulates net absorption of nutrients.

130. (New) A method for maintaining or restoring a function of a pancreatic islet, wherein the function is glucose responsivity or glucose sensing, comprising administering to a pancreatic islet, which pancreatic islet has impaired glucose responsivity or glucose sensing, a composition comprising a PYY agonist or a biologically active fragment thereof, wherein said PYY agonist comprises an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1, wherein the amount of said PYY agonist or biologically active fragment thereof is sufficient to maintain or restore the function of said pancreatic islet, and wherein said PYY agonist or biologically active fragment binds a PYY receptor.